UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/805,806	03/22/2004	Jeffrey S. Kiel	455-026	9957

1009 7590 09/20/2007

KING & SCHICKLI, PLLC
247 NORTH BROADWAY
LEXINGTON, KY 40507

EXAMINER	
OH, TAYLOR V	
ART UNIT	PAPER NUMBER
1625	

MAIL DATE	DELIVERY MODE
09/20/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/805,806	KIEL ET AL.	
	Examiner	Art Unit	
	Taylor Victor Oh	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Applicant's arguments with respect to claims 1-19 have been considered but are moot in view of the new ground(s) of rejection.

The Status of Claims

Claims 1-19 are pending.

Claims 1-19 are rejected.

DETAILED ACTION

1. Claims 1-19 are under consideration in this Office Action.

Priority

2. It is noted that this application claims benefit of 60/457,399 (03/25/03).

Drawings

3. None.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 17-19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not

described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification has merely mentioned that Gabapentin is a neuroleptic agent as adjunctive therapy in the treatment of central nervous system conditions in mammalian subjects , such as partial seizures, epilepsy, faintness attacks, hypokinesis, pain associated with shingles, and cranial trauma.

The specification falls short because data essential for how partial seizures, epilepsy, faintness attacks, hypokinesis, pain associated with shingles, and cranial trauma can be treated by means of administering Gabapentin to a patient with the above CNS disorders. This is because the CNS disorders can be caused by many different factors: inherited genetic abnormalities, problems in the immune system, injury to the brain or nervous system , diabetes , neuro-chemical imbalance (neurotransmitters), and etc.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

The Nature of the Invention

The nature of the invention in claims 17 is described below:

17. (currently amended) A method of treating a condition of the central nervous system in a mammalian subject wherein said condition of the central nervous system is selected from a group consisting of partial seizures, epilepsy, faintness attacks,hypokinesis, pain associated with shingles and cranial trauma, comprising administering a pharmaceutically effective amount of gabapentin tannate in solid dosage form.

The State of the Prior Art

The state of the prior art is that according to Drugs of Future (vol.9 no. 6, 1984p. 418-419),US Patent Nos. 5,095,148, 4,024,175, 4,152,326, and 5,132,451, Gabapentin has been used as an anticonvulsant to treat a patient. US Patent No. 5,068,413 describes that it is useful in therapy of certain cerebral disorders such as faintness attacks, hypokinesis and cranial traumas. Bennett et al (J Clin psychopharmacol. 1997, Arr., 17(2):141-2) discloses gabapentin for treatment of bipolar and schizoaffective disorders. Bozikas et al (Prog Neuropsychopharmacol Biol Psychiatry, 2002 Jan. 26 (1), :197-9) teaches treatment of alcohol withdrawal with gabapentin. And Brannon et al (Can J Psychiarty, 200 Feb; 45(1):84) has indicated that Gabapentin can be used for treating post-traumatic stress disorder.

However, there is no conclusive indicator that Gabapentin can be used for treating all the CNS diseases such as partial seizures, epilepsy, faintness attacks, hypokinesis, pain associated with shingles, and cranial trauma except some of them.

The predictability or lack thereof in the art

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art would recognize that the exact mechanism of gabapentin remains uncertain except that it is shown in recent data to be a selective agonist at the gb1a-gb2 heterodimer and post-synaptic $GABA_B$ receptor would result in only the specific receptor site of the brain cells; this kind of treatment can not be translated to the possible treatment of all the CNS diseases, such as partial seizures, epilepsy, faintness attacks, hypokinesis, pain associated with shingles, and cranial trauma in regards to their therapeutic effects.

Hence, in the absence of a showing of correlation between all the CNS diseases, such as partial seizures, epilepsy, faintness attacks, hypokinesis, pain associated with shingles, and cranial trauma claimed and treatment by the Gabapentin compound, one of skill in the art is unable to fully predict possible results from the administration of the claimed Gabapentin compound due to the unpredictability of the role of a selective agonist at the gb1a-gb2 heterodimer and post-synaptic $GABA_B$ receptor, i.e. whether promotion or inhibition would be beneficial for the treatment of all the CNS diseases.

There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The amount of direction or guidance present

The direction present in the instant specification is that the Gabapentin compound can treat some of the CNS diseases partial seizures, epilepsy, faintness attacks, hypokinesis, pain associated with shingles, and cranial trauma. However, the specification is silent and fails to provide guidance as to whether the CNS diseases listed (page 3, lines 21-23) requires the action of the Gabapentin for treatment, i.e. the specification fails to provide a correlation between the disease listed and the role of the Gabapentin. Also, there is no direction and guidance for the role of the Gabapentin for the treatment of the above CNS diseases.

The presence or absence of working examples

There is no working example for any of CNS diseases ,such as partial seizures, epilepsy, faintness attacks, hypokinesis, pain associated with shingles, and cranial trauma in the specification. Also, the Gabapentin compound disclosed in the specification has no pharmacological data regarding the treatment of the above CNS diseases except mentioning that it can treat a condition of the central nervous system in a mammalian subject and the specification has no data on the possible treatment of all the CNS diseases that require the action of the Gabapentin compound. Also, the specification fails to provide working examples as to how the listed diseases in the above can be treated by the action of the Gabapentin, i.e. again, there is no correlation between the diseases listed and the role of the Gabapentin.

The breadth of the claims

The breadth of the claims is that the Gabapentin can treat the above conditions of the central nervous system in a mammalian subject without regards as to the affect of the action of the Gabapentin on the stated disease.

The quantity of experimentation needed

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine what CNS diseases would be benefited by the action of the Gabapentin.

The level of the skill in the art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which one of CNS diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad use of the Gabapentin compound for the treatment of all the CNS diseases. As a result, necessitating one of skill to perform an exhaustive search for which CNS diseases can be treated by the Gabapentin compound in order to practice the claimed invention.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001 , states that " a patent is not a hunting license. It is not a reward for search , but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test which diseases can be treated by the compound encompassed in the instant claims, with no assurance of success.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or

improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 4-10 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1,3,5-8,11 of copending Application No. 10/269,027. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claim 1 is related to the process for preparing a gabapentin tannate pharmaceutical composition comprising mixing an anti-clumping agent , tannic acid together to form a reaction mixture ; adding gabapentin to said reaction mixture; and adding one or more solvents to said reaction mixture, whereas the claims 1,3 of the copending Application No. 10/269,027 is described below:

> 1. A process for the conversion of at least one active pharmaceutical ingredient into its tannate salt complex for incorporation into a therapeutic tablet, capsule or other solid dosage form, the process comprising:
>
> (a) combining, in the presence of a pharmaceutically acceptable liquid, the salt or free base of an active pharmaceutical ingredient with tannic acid to form a tannate salt complex of the active pharmaceutical ingredient and without further treatment; and
>
> (b) processing the tannate salt complex into a tablet, capsule or other solid dosage form.

3. The process according to claim 1, wherein the active pharmaceutical ingredient is selected from the group consisting of: (50) gabapentin

However, the instant invention differs from the copending Application No. in that the gabapentin tannate is not specified in the claim 1.

Even so, claim 3 describes that gabapentin can be one of the active pharmaceutical ingredients to be converted into its complex form with tannate salt. Therefore, it would have been obvious to the skillful artisan in the art to be motivated to rearrange the claims in such a way to emphasize the certain aspect of the claimed invention in the process because they are not patentably distinct from each other with respect to the claims of themselves. Furthermore, it is because claim 1 of the instant invention does fall into the scope of claim 1 in the copending application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 103

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Patel et al (US 6,248,363) in view of Gordziel (U.S. 6,037,358).

Patel et al discloses the general teachings of converting of one of the active pharmaceutical ingredients (hydrophilic, amphiphilic or hydrophobic) such as gabapentin (see col. 5, line 46) into its tannate salt complex (see col. 40, line 7) as a salt of a pharmaceutically acceptable cation (see col. 39 , line 65).

The instant invention, however, differs from the prior art reference in that mixing an anti-clumping agent and tannic acid together in the presence of isopropyl alcohol is not disclosed ; the anti-clumping agent is at a concentration of 0.001 to 95 % by wt of the composition.

Gordziel discloses a process of preparing antihistamine tannates ; for example , chlorpheniramine tannate can be obtained from reacting chlorpheniramine with tannic acid in the presence of isopropanol (see col. 1 , lines 64-67). Furthermore, the following example is further exemplified as shown below (see col. 2 , ex. 1):

EXAMPLE 1

Ingredient	Milligrams per Tablet
Chlorpheniramine Tannate	9.0
Phenylephrine Tannate	25.0[1]
Starch, NF	65.0
Methylcellulose, USP	150
Polygalactouronic Acid	32.0
Dibasic Calcium Phosphate, USP, Dihydrate	65.0
Povidone, USP	25.0
Talc, USP	5.4
FD&C Red #40 Aluminum Lake-40%	3.93
D&C Blue #1 Aluminum Lake-29%	1.0
Magnesium Stearate, NF	4.0
Alcohol Specially Denatured 23A 190 Proof	140[2]

[1]15% excess added during manufacture
[2]Not present in finished tablet product

Patel et al expressly discloses that it seems reasonable to convert the active pharmaceutical ingredients such as chlorpheniramine (see col. 5, line 34), gabapentin (see col. 5, line 46) into its tannate salt complex. Similarly, Gordziel does teach the process of preparing pure antihistamine tannate compositions by reacting chlorpheniramine with tannic acid in the presence of isopropanol. By comparison, there is an equivalency between chlorpheniramine

tannate and gabapentin tannate with respect to preparing the their corresponding tannate pharmaceutical forms between the prior art.

Therefore, if the skilled artisan had desired to convert the active gabapentin pharmaceutical ingredient into its tannate salt complex as an alternative to the chlorpheniramine tannate composition, one skilled in the art would be motivated to incorporate Gordziel's anti-clumping process of preparing the tannate composition into the Patel et al process. This is because the skilled artisan in the art would expect such a combination to be successful in producing gabapentin tannate as the guidance that the active hydrophilic ,lipophilic, amphiphilic or hydrophobic ingredient can be solubilized in the encapsulation shown in the Patel et al process.

Claims 11-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bryans et al (US 7,141,606) in view of Berge et al (J. of Pharmaceutical Sciences, 66,no. 1, Jan, 1977, p.1-19).

Bryans et al discloses gabapentin derivatives having the following uses(see col. 1, lines 22-26):

> protective effect against cramp induced by thiosemicarbazide; protective action against cardiazole cramp; the cerebral diseases, epilepsy, faintness attacks, hypokinesia, and cranial traumas; and improvement in cerebral functions. The

For preparing pharmaceutical compositions from the compounds of the present invention, pharmaceutically acceptable carriers can be either solid or liquid. Solid form preparations include powders, tablets, pills, capsules, cachets, suppositories, and dispersible granules. A solid carrier can be one or more substances which may also act as diluents, flavoring agents, binders, preservatives, tablet disintegrating agents, or an encapsulating material.

In powders, the carrier is a finely divided solid which is in a mixture with the finely divided active component.

In tablets, the active component is mixed with the carrier having the necessary binding properties in suitable proportions and compacted in the shape and size desired.

The powders and tablets preferably contain from five or ten to about seventy percent of the active compound. Suitable carriers are magnesium carbonate, magnesium stearate, talc, sugar, lactose, pectin, dextrin, starch, gelatin, tragacanth, methylcellulose, sodium carboxymethylcellulose, a low melting wax, cocoa butter, and the like. The term "preparation" is intended to include the formulation of the active compound with encapsulating material as a carrier providing a capsule in which the active component, with or without other carriers, is surrounded by a carrier, which is thus in association with it. Similarly, cachets and lozenges are included. Tablets, powders, capsules, pills, cachets, and lozenges can be used as solid dosage forms suitable for oral administration.

Liquid form preparations include solutions, suspensions, and emulsions, for example, water or water propylene glycol solutions. For parenteral injection liquid preparations can be formulated in solution in aqueous polyethylene glycol solution.

(see col. 12, lines 4-45)

The quantity of active component in a unit dose preparation may be varied or adjusted from 0.1 mg to 1 g according to the particular application and the potency of the active component. In medical use the drug may be administered three times daily as, for example, capsules of 100 or 300 mg. The composition can, if desired, also contain other compatible therapeutic agents.

(see col. 13, lines 1-7).

Furthermore, the gabapentin has a nitrogen and a carboxyl group in the chemical compound and its salt possible forms are described in the followings (see col. 10 ,lines 33-37):

> Since amino acids are amphoteric, pharmacologically compatible salts when R is hydrogen can be salts of appropriate inorganic or organic acids, for example, hydrochloric, sulphuric, phosphoric, acetic, oxalic, lactic, citric, malic, salicylic, malonic, maleic, succinic, methanesulfonic acid,

However, the instant invention differs from the prior art in that the formation of gabapentin tannate is undisclosed in the prior art.

Berge et al describes potentially useful salts in the pharmaceutical compounds in which the salt is formed by an acid-base reaction involving either a proton-transfer or neutralization reaction (see page 2 , left col. at the middle paragraph). Furthermore the table I shows various FDA-approved commercially marketed salts among which the tannate is displayed as one of the potential candidates for the pharmaceutical compounds.

Bryans et al expressly discloses that it seems reasonable to form the organic salt forms of gabapentin for sleep disorders (see col. 10 ,lines 33-37). Berge et al expressly describes various FDA-approved commercially marketed salts among which the tannate is displayed as one of the potential candidates for the pharmaceutical compounds. Therefore, it would have been obvious to the skillful artisan in the art to be motivated to use the tannate for the salt of gabapentin for sleep disorders ; this is because Berge et al expressly teaches that one of the FDA-approved commercially marketed salts can be the tannate.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taylor Victor Oh whose telephone number is 571-272-0689. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Taylor Victor Oh, MSD,LAC
Primary Examiner
Art Unit : 1625

*** 9/18/07